

Brief Description of the Drawings:

Figure 1: SDS-PAGE:

St = Standards

E4, C11, B3, B9, G6, G9 = anti-id BR55-2 Mabs

Figure 2: Isoelectric Focussing:

St = Standard

R = Reference Mab

E4, C11, B3, B9, G6 and G9 = anti-id BR55-2 Mabs

Figure 3: Binding of BR55-2/murine IgG3 to SKBR5 cell line

Inhibition by anti-id BR55-2 #E4

BR55-2/murine IgG3: 1 µg/ml

Figure 4: Binding of rabbit Ig to SKBR5 before and after immunization with anti-id BR55-2 #E4 (Cell-ELISA)

—+— before immunization

—□— week 9 after immunization

Figure 5: Binding of rhesus monkey Ig to SKBR5 before and after immunization with

anti-id BR55-2 #E4 (Cell-ELISA)

—+— before immunization

—□— week 9 after immunization

Figure 6: Immunization of monkey 246 with anti-id BR55-2 #E4

Serum Ig binding to anti-id BR55-2 #E4 (ELISA)

—□— 246 pre

—□— 246 week 4

—○— 246 week 9

—△— 246 before 1st boost

—○— 246 week 1 after 2nd boost

—+— 246 before 2nd boost

—△— 246 week 4 after 2nd boost

—■— 246 week 9 after 2nd boost

Figure 7: Immunization of monkey 287 with anti-id BR55-2 #E4
Serum Ig binding to anti-id BR55-2 #E4 (ELISA)

—□— 287 pre

—□— 287 week 4

—○— 287 week 9

—△— 287 before 1st boost

—◇— 287 week 4 after 1st boost

—✦— 287 before 2nd boost

—△— 287 week 4 after 2nd boost

—■— 287 week 9 after 2nd boost

Figure 8: Immunization of monkey E23 with anti-id BR55-2 #E4
Serum Ig binding to anti-id BR55-2 #E4 (ELISA)

—□— pre

—□— week 4

—○— week 9

—△— before 1st boost

—◇— week 4 after 1st boost

—✦— before 2nd boost

—○— week 1 after 2nd boost

—△— week 4 after 2nd boost

—■— week 9 after 2nd boost

Figure 9: Immunization of monkey 215 with irrelevant mouse IgG1
Serum Ig binding to anti-id BR55-2 #E4 (ELISA)

- B₂
- 215 pre
 - 215 week 4
 - 215 week 9
 - △— 215 before 1st boost
 - 215 week 1 after 1st boost
 - ◇— 215 week 4 after 1st boost
 - ✕— 215 before 2nd boost
 - 215 week 1 after 2nd boost
 - ▲— 215 week 4 after 2nd boost
 - 215 week 9 after 2nd boost

Figure 10: Immunization of monkey 252 with irrelevant mouse IgG1
Serum Ig binding to anti-id BR55-2 #E4 (ELISA)

- pre
- week 9
- ✕— before 2nd boost
- week 9 after 2nd boost

Figure 11: Immunization of monkey 246 with anti-id BR55-2 #E4

Serum Ig binding to SKBR5 breast cancer cells (cell-ELISA)

- pre
- week 9

- △— before 1st boost
- ◇— week 4 after 1st boost
- ☆— before 2nd boost
- △— week 4 after 2nd boost
- week 9 after 2nd boost

Figure 12: Immunization of monkey 287 with anti-id BR55-2 #E4

Serum Ig binding to SKBR5 breast cancer cells (cell-ELISA)

- pre
- ★— week 1
- week 4
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ☆— before 2nd boost
- week 1 after 2nd boost
- △— week 4 after 2nd boost
- week 9 after 2nd boost

Figure 13: Immunization of monkey E23 with anti-id BR55-2 #E4

Serum Ig binding to SKBR5 breast cancer cells (cell-ELISA)

- pre
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ☆— before 2nd boost
- week 1 after 2nd boost
- △— week 4 after 2nd boost
- week 9 after 2nd boost

Figure 14: Immunization of monkey 215 with irrelevant mouse IgG1
Serum Ig binding to SKBR5 breast cancer cells (cell-ELISA)

- pre
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ☆— before 2nd boost
- ⊥— week 4 after 2nd boost
- ⊞— week 9 after 2nd boost

Figure 15: Immunization of monkey 246 with anti-id BR55-2 #E4

Serum Ig binding to CATO gastric cancer cells (cell-ELISA)

- pre
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ☆— before 2nd boost
- ⊞— week 9 after 2nd boost

Figure 16: Immunization of monkey 215 with irrelevant mouse IgG1
Serum Ig binding to CATO gastric cancer cells (cell-ELISA)

- pre
- week 9

- △— before 1st boost
- ◇— week 4 after 2nd boost
- ✦— before 2nd boost
- ⊠— week 9 after 2nd boost

Figure 17: Immunization of monkey E23 with anti-id BR55-2 #E4
Serum Ig binding to SW2 small cell lung cancer cells (cell-ELISA)

- pre
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ✦— before 2nd boost
- △— week 4 after 2nd boost
- ⊠— week 9 after 2nd boost

Figure 18: Immunization of monkey 215 with irrelevant mouse IgG1
Serum Ig binding to SW2 small cell lung cancer cells (cell-ELISA)

- pre
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ✦— before 2nd boost
- △— week 4 after 2nd boost
- ⊠— week 9 after 2nd boost

Figure 19: Immunization of monkey E23 with anti-id BR55-2 #E4

Serum Ig binding to SW 948 colon cancer cells (cell-ELISA)

- pre
- week 9
- △— before 1st boost
- ◇— week 4 after 1st boost
- ◊— before 2nd boost
- ☆— week 4 after 2nd boost
- ⊠— week 9 after 2nd boost

Figure 20: Immunization of monkey E23 with anti-id BR55-2 #E4

Serum Ig binding to WM9 melanoma cells (cell-ELISA)

- pre
- week 9
- ☆— before 1st boost
- ◇— week 4 after 2nd boost
- ⊠— before 2nd boost
- ⊠— week 9 after 2nd boost

Figure 21: Rhesus monkey Ig immunopurified on anti-id BR55-2 #E4*:

- immuno-purified Ig (AB3)
- flow through

* Rhesus monkey 246:
pooled serum of week 4
and 9 after 2nd boost

Figure 22: Rhesus monkey Ig immunopurified on anti-id BR55-2 #E4*:
binding to SKBR5 breast cancer cells (cell-ELISA)

* Rhesus monkey 246:
pooled serum of week 4 and 9
after 2nd boost

Figure 23: Rhesus monkey Ig immunopurified on anti-id BR55-2 #E4*:
binding WM9 (melanoma) and SKBR5 (breast cancer) cells (cell-ELISA)

- WM9 (AB3)
- SKBR5 (AB3)
- WM9 (humanized AB1)
- SKBR5 (humanized AB1)

* Rhesus monkey 246:
pooled serum of week 4
and 9 after 2nd boost

Figure 24: Rhesus monkey Ig immunopurified on anti-id BR55-2 #E4*:
binding to SKBR5 – and WM9 – cell membranes (ELISA)

- purified Ig (SKBR5)
- purified Ig (WM9)

* Rhesus monkey 246:
pooled serum of week 4 and 9
after 2nd boost

Figure 25: Rhesus monkey Ig immunofuried on anti-id BR55-2 #E4*:
binding to different cell lines (cell-ELISA)

- SW2
- CATO
- ★— SKBR5
- ◇— SW948

* Rhesus monkey 246:
pooled serum of week 4
and 9 after 2nd boost

Figure 26: ADCC to SKBR5 breast cancer cell line mediated by human PBMC and
BR55-2/murine IgG3 or immunopurified Ig of a rhesus monkey*
immunized with ati-id BR55-2 #E4

- Immunopurified monkey Ig (AB3)
- ▣ BR55-2/murine IgG3 (AB1)

*) rhesus monkey 246: serum of week 9
after start of immunization

E:T = 15:1

Figure 27: ELISA for the dertermination of BR55-2/murine IgG3 in
human serum – standard curve

Figure 28: ELISA for the determination of BR55-2/chimeric human IgG1
in human serum – standard curve

Figure 29: ELISA for the determination of BR55-2/chimeric human IgG3
in human serum – standard curve

Figure 30: Binding of BR55-2/chimeric IgG1 and BR55-2/humanized IgG1
to anti-id BR55-2 #E4

- BR55-2/chimeric IgG1
- BR55-2/humanized IgG1

B₂
Figure 31: Binding of BR55-2/chimeric IgG1 and BR55-2/humanized IgG1
to anti-id BR55-2 #C11

- BR55-2/chimeric IgG1
- BR55-2/humanized IgG1

Figure 32: Binding of BR55-2/chimeric IgG1 and BR55-2/humanized IgG1
to anti-id BR55-2 #B3

- BR55-2/chimeric IgG1
- BR55-2/humanized IgG1

Figure 33: Binding of BR55-2/chimeric IgG1 and BR55-2/humanized IgG1
to anti-id BR55-2 #B9

- BR55-2/chimeric IgG1
- BR55-2/humanized IgG1

Figure 34: Binding of BR55-2/chimeric IgG1 and BR55-2/humanized IgG1 to anti-id BR55-2 #G6

- BR55-2/chimeric IgG1
- BR55-2/humanized IgG1

Figure 35: Binding of BR55-2/chimeric IgG1 and BR55-2/humanized IgG1 to anti-id BR55-2 #G9

- B₂
- BR55-2/chimeric IgG1
 - BR55-2/humanized IgG1

Figure 36: ELISA for the determination of BR55-2/humanized IgG1 in human serum – standard curve

Figure 37: Binding competition of BR55-2/murine IgG3 to anti-ID BR55-2 by BR55-2/chimeric human IgG1 and BR55-2/chimeric human IgG3

- *— BR55-2/chimeric IgG1
- +— chimeric human IgG1*
- 0.05 µg/ml mIgG3
- ◇— chimeric human IgG3*
- 0.05 µg/ml mIgG3

Figure 38: Complement dependent cytotoxicity mediated by BR55-2/murine IgG3
Inhibition by anti-ID BR55-2 E4

B₂
BR55-2/murine IgG3: 1.4 µg/ml

Figure 39: SDS-Page. Reducing conditions:

St = Standards

R = Reference Mab

Ch = BR55-2/chimeric human IgG1

IN THE CLAIMS:

Please cancel claims 1-12 without prejudice or disclaimer of the subject matter contained therein.

Please enter new claims 13-28 as set forth below:

- B₃
13. (New) A monoclonal murine internal image anti-idiotypic antibody (Ab2) to monoclonal antibodies BR55-2 (Ab1) having an inhibition capacity of more than 95% in terms of inhibition of binding of BR55-2